REMARKS

Claims 39-58, 62, 80, 82, 89, 91 and 97-100 are pending in this application. Claim 39 has been amended to further clarify the invention. This amendment finds support in paragraphs 16, 17, 21, 23, and 45 of the published specification. No new subject matter has been introduced by this amendment.

The amendment has been made solely to further prosecution of the instant application. Applicants respectfully request reconsideration in view of the claim amendments and the following remarks.

Response to 35 U.S.C. §102 Rejections

Claims 39-44, 55, 56, 62, 89, 91, and 97 have been rejected under 35 U.S.C. §102(b) as being anticipated by Gossen, et al. (U.S. 5,602,300). Applicants respectfully disagree.

MPEP §2131 states that in order for a reference to anticipate a claim under 35 U.S.C. §102, the reference must teach each and every element of the claim. Gossen describes two main methods which require the protein or proteinacious material is bound to the solid particles (i.e., the matrix) using a ß-galactosidase antibody (see Gossen et al., column 4, lines 13-27). The nucleic acids are then exposed to the matrix whereby the protein then binds the target molecules to enable separation of the nucleic acid populations. In the instant invention the protein is bound to the nucleic molecules ("tagged"), either directly or indirectly, prior to exposure of the tagged nucleic acids to the matrix (see paragraphs 16, 17, 21, 23 and 45 of the published specification). The matrix then binds the protein thereby selecting the "unwanted" molecules to eliminate

them from the solution thereby enabling the selection of the target nucleic acid molecules. The Gossen reference does not teach or suggest how one of ordinary skill in the art would tag the nucleic acids used in the claimed methods and therefore does not enable the claimed methods. An anticipatory reference must be enabled. *Impax Labs., Inc. v. Aventis Pharm. Inc.,* 468 F.3d 1366, 1381 (Fed. Cir. 2006).

Claim 39 has been amended to further clarify the instant invention. The application supports this amendment by describing that the protein is bound, either directly or indirectly, with the nucleic acid molecules prior to being exposed to the matrix for the separation step. Gossen et al. does not teach or suggest this essential step. Rather, Gossen describes that the protein is bound to the matrix but NOT to the nucleic acid. Since Gossen does not teach each and every element of claim 39, Gossen does not anticipate claim 39 under 35 U.S.C. §102.

Applicants believe that Gossen does not teach or suggest the claimed invention because the reference does not tag the nucleic acid population prior to exposing it to the solid matrix. Because the Gossen reference does not anticipate the independent claim, the reference cannot anticipate the dependent claims. Applicants submit that for this reason independent claim 39 as well as all of the dependent claims 40-44, 55-56 and 97 are believed allowable.

For the above reasons, and in view of the claim amendments, applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §102(b) for the above reason.

Response to 35 U.S.C. §103 Rejections

Gossen in view of Seed

Claims 45, 46, 80, 82, and 99 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Gossen et al. (U.S. 5,602,300) as applied to claims 39, 43, and 44 above, and further in view of Seed (EP 0580305 A2). Applicants respectfully traverse this rejection.

As discussed above, amended claim 39 contains at least one feature that is not disclosed in Gossen; the DNA plasmid referred to in Gossen is not tagged with a protein prior to its interaction with the matrix. There is no teaching or suggestion in Gossen to tag a nucleic acid population with a protein; and thereafter to isolate that population of tagged molecules on a matrix. Because Gossen uses a lac Z operator nucleic acid sequence as the means to facilitate nucleic acid-protein interaction, every target sequence must contain that particular nucleic acid motif. In contrast, the present invention discloses a means for tagging the target population with a protein so that specific nucleic acid sequences are not required for the invention as claimed. Gossen does not teach or suggest how one skilled in the art could tag the target nucleic acid population prior to its interaction with a matrix. Additionally, Gossen discloses the use of solid particles which are pre-bound with either a lac Z operator binding material or a ß-galactosidase antibody. The tag in Gossen is attached to the matrix and not the nucleic acid sequence.

As mentioned by the Examiner, Seed describes a matrix for separating nucleic acids in a cartridge device. Seed does not, however, teach or suggest the tagging of a nucleic acid population with a protein prior to its exposure to a matrix.

Neither Gossen nor Seed teach or suggest that the nucleic acids are pre-bound to a protein tag as required by the instant claims. Therefore, applicants respectfully assert that a *prima facie* case of obviousness for these claims has not been made out with respect to Gossen in view of Seed. Additionally, neither Gossen nor Seed provide a motivation or reason to place the protein tag on the nucleic acid molecules prior to exposing the nucleic acid molecules to the matrix thereby selectively binding the tag. See MPEP §2144.04. Therefore, applicants respectfully request reconsideration and withdrawal of this §103(a) rejection.

Gossen in view of Davis

Claims 47-54 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Gossen et al. (U.S. 5,602,300) as applied to claim 39 above, and further in view of Davis et al. (WO 90/12115). Applicants respectfully traverse this rejection.

Claims 47-54 are all dependent, directly or indirectly, on claim 39. As discussed above, the DNA plasmid referred to in Gossen is not tagged with a protein tag prior to its exposure to the matrix as claimed. The tag in Gossen is attached to the matrix and not to the nucleic acid sequence.

There is no teaching or suggestion in Gossen to tag a nucleic acid population with a protein tag prior to its interaction with a matrix. In contrast, Gossen describes the use of solid particles to which are bound lac Z operator binding material or repressor; and the use of such particles to isolate plasmids containing a particular nucleic acid sequence, *i.e.*, the lac Z operator. The Examiner has not given any reasons how a person of ordinary skill in the art would arrive at the method as claimed, which requires

labeling the nucleic acid population prior to interaction with a matrix, from a reference which does not teach or suggest to do so.

Davis relates to the amplification of DNA fragments by using the polymerase chain reaction technique (PCR) and the detection of mutations. However, Davis does not teach or suggest the tagging of a nucleic acid population with a protein prior to exposure to a matrix in a sequence independent manner.

Neither Gossen nor Davis teach or suggest that the tag must be attached to the nucleic acid molecules as required by the present invention. Therefore, applicants respectfully assert that a *prima facie* case of obviousness for these claims has not been made out with respect to Gossen in view of Davis. Hence, applicants respectfully request reconsideration and withdrawal of this §103(a) rejection.

Gossen in view of Dower

Claims 57 and 58 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Gossen et al. (U.S. 5,602,300) as applied to claim 39 above, and further in view of Dower et al. (U.S. 5,427,908). Applicants respectfully traverse this rejection.

Claims 57 and 58 are dependent on claim 39. Claims 57 and 58 are specifically directed at *in vitro* packaging of nucleic acids that have been separated by the method described in claim 39 into bacteriophage particles.

Dower relates to the *in vitro* packaging of bacteriophage particles. However, Dower does not teach or suggest the tagging of a nucleic acid population with a protein prior to its exposure to a matrix as required by all of the instant claims. Dower

describes a general *in vitro* packaging technique for bacteriophage particles, however neither Gossen nor Dower describe a method of selectively separating a tagged population of nucleic acid molecules wherein the nucleic acid molecules are tagged prior to exposure to the matrix. Therefore, Dower is inadequate to remedy the deficiencies of Gossen and therefore cannot render the instant claims obvious.

Neither Gossen nor Dower alone or in combination teach or suggest that the tag must be attached to the nucleic acid molecules prior to exposing these molecules to the matrix as required by the instant claims. Therefore, applicants respectfully submit that a *prima facie* case of obviousness for these claims has not been established with respect to Gossen in view of Dower. Hence, applicants respectfully request reconsideration and withdrawal of this §103(a) rejection.

Gossen in view of Sano

Claim 98 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Gossen et al. (U.S. 5,602,300) as applied to claims 39 and 97 above, and further in view of Sano et al. (U.S. 5,665,539). Applicants respectfully traverse this rejection.

Claim 98 is dependent on claims 39 and 97. Claim 98 is specifically directed at a method wherein the proteins are linked to or attached to the nucleic acid molecules using a biotin-streptavidin interaction.

As discussed above, there is no teaching or suggestion in Gossen to tag a nucleic acid population with a protein prior to exposure to a matrix. The protein in the Gossen reference is attached to the matrix and not the nucleic acid molecule. Gossen does not provide any motivation or suggestion to bind the protein to the nucleic acid

molecules. One of ordinary skill in the art would not be motivated to make such a change in Gossen's method.

Sano describes a method of detecting antigens by using specific antigen-antibody-marker conjugates. Although this method teaches the use of a biotin-streptavidin interaction to bind specific DNA molecules, there is no reason that one of ordinary skill in the art would combine this teaching with Gossen, because the gist of these methods are completely opposite. Gossen targets the matrix for placement of the protein whereas Sano places the tag on the DNA molecules directly. There is no reason to switch the binding target.

MPEP §2143.01 states that "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." The method described in Gossen is used to separate out targeted nucleic acid molecules. It is essential that the nucleic acid molecules can be extracted from the matrix in order to proceed with the remaining steps of the Gossen method. Sano describes a biotin-streptavidin linkage for targeting nucleic acids, however the streptavidin binds almost irreversibly to any molecule that contains biotin (see col. 4, lines 63-65). Thus, one of ordinary skill in the art would not modify the Gossen method by combining these references because they would fear that the biotin-streptavidin linkage would be too strong to break in order to isolate the targeted nucleic acid molecules. The Gossen method focuses on targeting specific nucleic acid molecules for further processing (see col. 3, lines 3-13). Sano describes a method in which the biotin-streptavidin system is used to detect antigens. The method in Sano does not require that the nucleic acids be released from the streptavidin-biotin tag; once

the antigen is attached via the streptavidin-biotin interaction a segment of the nucleic acid is amplified for detection (see col. 3, lines 29-38). Hence, one of ordinary skill in the art would not be motivated to combine Gossen and Sano since it is not desirable to irreversibly bind the tag to the nucleic acid molecules in Gossen.

Since there is no motivation to combine Gossen with the teachings of Sano to achieve the method claimed, applicants respectfully request reconsideration and withdrawal of this §103(a) rejection.

Gossen and Seed in view of Sano

Claims 99 and 100 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Gossen et al. (U.S. 5,602,300) and Seed (EP 0580305 A2) as applied to claims 39, 43, 44, and 80 above, and further in view of Sano et al. (U.S. 5,665,539). Applicants respectfully traverse this rejection.

Claims 99 and 100 are dependent on claims 80 and 99 respectively. Claim 99 is drawn to a method of separating nucleic acid molecules by using a protein that is linked or attached to nucleic acid molecules. Claim 100 is drawn to the method in claim 99 wherein the proteins are linked to the nucleic acid molecules with a biotin-streptavidin complex.

As discussed above, neither Gossen nor Seed teach or suggest that the nucleic acid population be tagged with a protein prior to exposure to a matrix as required by the present invention. Therefore, applicants respectfully assert that a *prima facie* case of obviousness for these claims has not been established with respect to Gossen in view of Seed. Additionally, neither Gossen nor Seed provide a motivation or reason to place

the protein tag, directly or indirectly, on the nucleic acid molecules prior to exposing the nucleic acid molecules to the matrix which then selectively binds the tag. See MPEP §2144.04.

As previously discussed, the methods in Gossen and Sano are completely opposite, Gossen targets the matrix for placement of the protein tag wherein Sano places a tag on the DNA molecules directly. There is no motivation to combine these references because the gist of these methods are completely unrelated. It is essential that the nucleic acid molecules can be extracted from the matrix in order to proceed with the remaining steps of the Gossen method. Sano describes a biotin-streptavidin linkage for targeting nucleic acids, however the streptavidin binds almost irreversibly to any molecule that contains biotin. Hence, one of ordinary skill in the art would not be motivated to combine Gossen and Sano since it is not desirable to irreversibly bind the tag to the nucleic acid molecules in Gossen.

Since there is no motivation to combine Gossen and Seed with the teachings of Sano to achieve the invention contained in the instant claims, the applicants respectfully request reconsideration and withdrawal of this §103(a) rejection.

CONCLUSION

Based on the foregoing amendments and remarks, applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **13-4500**, Order No. 4290-4000. A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **13-4500**, Order No. 4290-4000. A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

Respectfully submitted,
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Dated: February 28, 2007 By: _____
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